Insulin resistance and liver damage are associated with early signs of left ventricular systolic dysfunction in patients with Non Alcoholic Fatty Liver Disease independent of diabetes, hypertension and dyslipidemia

RS-3519
Fatty liver disease
Clinical

INSULIN RESISTANCE AND LIVER DAMAGE ARE ASSOCIATED WITH EARLY SIGNS OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE INDEPENDENT OF DIABETES, HYPERTENSION AND DYSLIPIDEMIA.

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Background and Aims: Nonalcoholic Fatty Liver Disease (NAFLD) has been associated with subclinical cardiovascular disease (CVD). This study was undertaken to evaluate the relationship between metabolic parameters, histologic features and parameters of cardiac morphology and function in NAFLD subjects.

Methods: Nineteen non-diabetic, non-dyslipidemic, non-hypertensive patients with biopsy-proven NAFLD (17 men, age 41±8 years, BMI 26.8±3kg/m^2) and 9 healthy controls (5 men, age 30±2 years, BMI 22.5±2kg/m^2) underwent transthoracic echocardiography and cardiac MRI to evaluate cardiac morphology and function. Endogenous glucose production (EGP) and lipolysis were assessed by stable isotope tracers. Hepatic Insulin resistance (IR) as EGP x fasting insulin, Oral Glucose Insulin Sensitivity (OGIS), adipo-IR as free fatty acids (FFAs) x fasting insulin were calculated.

Results: Despite the absence of diabetes, hypertension and overt dyslipidemia, NAFLD patients had significantly higher concentration of FFAs than controls ($p<0.05$) and higher total saturated and monounsaturated levels ($p<0.05$). In NAFLD basal Hepatic-IR (NAFLD vs controls: 92±34 vs 52±18 umol/min kg*mU/L) and Adipo-IR (NAFLD vs controls: 21±10 vs 11±5 mmol/L*mU/L) were significantly increased ($p<0.03$ for all NAFLD vs controls) and OGIS significantly reduced (NAFLD vs controls: 11.0±1.64 vs 13.1±1.1 mg/kg min, $p=0.005$). The end-systolic LV diameter (30.4±3.7 vs 27.2±3.5 mm, $p=0.044$) was significantly higher in patients than in controls, suggesting subclinical systolic dysfunction. In NAFLD patients, both hepatic-IR and adipo-IR directly correlated with MRI end-systolic LV volume (ESV) ($r=0.63$, $p=0.004$ and $r=0.54$, $p=0.018$, respectively), while OGIS was inversely related to end-systolic LV diameter ($r=-0.48$, $p=0.037$) and ESV ($r=-0.48$, $p=0.036$). At liver biopsy, steatosis ≥33% was associated with increased ESV ($p=0.047$), suggesting early systolic dysfunction. Similarly, ESV was increased in patients with fibrosis (69.2±16.9 vs 94.5±31.4 cc, $p=0.018$), whereas the ejection fraction (51±7 vs 59±7%, $p=0.034$) and cardiac index (2.9±0.7 vs 3.8±0.9, $p=0.03$) were significantly reduced.

Conclusions: In NAFLD subjects metabolic derangements and histological features are associated with subclinical systolic LV dysfunction independent of diabetes, hypertension and dyslipidemia.

Funded by FP7/2007-2013 under grant agreement n HEALTH-F2-2009-241762 for the project FLIP and by PRIN 2009ARYX4T

Disclosure of Interest: None Declared